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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/066,498	01/30/2002	Jong-Gu Park	57354-00002	5213

7590 07/13/2005

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EXAMINER	
SCHULTZ, JAMES	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 07/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/066,498	PARK ET AL.	
	Examiner	Art Unit	
	J. D. Schultz, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-39,46,47 and 50-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-39,46,47 and 50-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 22 April 2005 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 28 July 2004 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 30-39, 46, 47 and 50-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellmann et al., in view of Moon et al., LaPlante et al., Hu et al. (all of record), and Gewirtz *et al.* (Proc. Natl. Acad. Sci. 1996. v 93, pp.3161-3163), and is repeated for the same reasons of record as set forth 22 April 2005.

At the outset, it is noted that claims 38, 46, and 47 were previously rejected as being obvious over Hellmann in view of Moon and LaPlante in the previous office action mailed 28 July 2004. Because said previous rejection falls directly under the scope of the instant rejection (i.e. the same claims rejected under the same stature using the same art), and in an effort to avoid redundancy, said previous rejection is withdrawn, in view of the fact that the claims remain rejected under the same statute and with the same art. It is emphasized that the withdrawal of the rejection of claims 38, 46, and 47 as being obvious has been made merely to simplify the issues; the art as cited is still considered to apply to said claims for the same reasons of record as set

forth 22 April 2005, and as explained below. Therefore, withdrawal of one rejection against claims 38, 46, and 47 in favor of another does not constitute a suggestion that the claims are not obvious over the prior art cited.

Regarding the rejection that is presently maintained, Applicants assert that while Hellmann indeed teaches a large circular single-stranded nucleic acid molecule comprising at least one target specific antisense region that is effective for reducing expression of said gene, Hellmann lacks the transfection reagents as claimed instantly. Applicants assert therefore that "the reach and limit of the disclosure of the Hellmann reference is the cell-free system". However, it is well established that a prior art reference is available for all that it fairly teaches or suggest to one of ordinary skill in the art. Since Hellmann teaches antisense inhibition of target expression, one of ordinary skill in the antisense art would understand that it is obvious to combine such compounds with transfection agents such as those claimed instantly. This is evidenced by the secondary references of Moon, LaPlante, and Hu, all of whom teach transfection of circular nucleic acids relating to antisense inhibitors into cells using transfection reagents. Thus while Hellmann may not teach a transfection reagent, Hellmann was not relied upon for this. It is the references of Moon, LaPlante, and Hu that directly teach that transfection agents are commonly used in compositions comprising antisense inhibitors. Since Hellmann teaches antisense inhibition, Applicants' assertions that the reach and limit of the disclosure of the home and reference is the cell free system are not convincing because one of ordinary skill in the antisense art would understand that Hellmann does not teach away from the use of such inhibitors, and because one of skill in the antisense art would have viewed Hellmann in view of

Moon, LaPlante, and Hu as suggesting the use of large circular nucleic acids, and would have known that the use of such transfection agents with such compounds are common adopted.

Applicants argue that each of Moon, LaPlante, and Hu separately fail to disclose or suggest the presently claimed inventive composition. However, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants argue that Hellmann is not combinable with Moon, LaPlante, Hu, or Gewirtz, because Hellmann discloses only a cell free system, which according to Applicants, presents a separate and unique challenge from the systems of Moon LaPlante and Hu, which are cell based. Applicants conclude that the Hellmann and Moon references are thus not analogous art and are not combinable. This basis for asserting that Hellmann and Moon are not analogous art is not convincing, because both Hellmann and Moon use large circular nucleic acids to inhibit gene expression, and therefore, not only are they considered analogous, they are also considered to have significant literal overlap in their teachings. Although Hellmann's method is taught in a cell free system, which contrasts with the cell based system of Moon, the fact that both use large circular nucleic acids comprising antisense regions to inhibit the expression of a specific target gene would suggest to one of ordinary skill in the antisense art that these references are indeed combinable.

Although Moon teaches the use of cationic liposomes to enhance the cellular uptake of relatively large single-stranded circular nucleic acids comprising in antisense region, applicants

argue that Moon alone does not suggest that successful transfection can take place with a large circular single-stranded nucleic acid that is at least 3000 bases long, because the oligos of Moon are only 116 nucleotides long. Even if this point were to be granted, which it is not, this argument ignores the fact that LaPlante and Hu both teach transfection of large plasmids that are at least about 3000 nucleotides long using transfection agents identical to that claimed instantly. Furthermore, the assertion that Moon fails to suggest that transfection of large nucleic acids at least about 3000 nucleotides long would be successful is contradicted by the statement by the statement in Moon at page 4652, "from the experience of our own and other groups, a meaningful level of AS all ago uptake should be consistently attainable when carried into cells by liposomes, *regardless of the size of AS oligos* (31, 32)." (Emphasis added).

The LaPlante disclosure is asserted by applicants to fail to provide any motivation to transfect a large circular single-stranded nucleic acid molecule. However, LaPlante discloses transfection of a target specific antisense cDNA. This is the feature for which LaPlante is relied upon. The fact that LaPlante doesn't teach said antisense as a circular nucleic acid was *not* a feature for which LaPlante was relied upon. The limitation of "circular" is taught by Moon, as well as Hellmann, both of which also teach antisense mediated inhibition. Therefore, Applicants' arguments that Hellmann and LaPlante are not analogous is not convincing, merely because Hellmann uses a cell free assay whereas LaPlante utilizes a cell based assay. Both references utilize large antisense nucleic acids for target specific inhibition.

Applicants also assert that Hellmann fails to be combinable with Hu, because "Hu is mainly concerned with optimizing expression of its antisense RNA producing method and its effectiveness within a cell" (applicants arguments page 10). Applicants reiterate their belief that

Hellmann's cell free system renders it non-combinable with a reference such as that of Hu, which teaches cellular antisense-mediated inhibition. Again, these arguments are not considered convincing, because both the Hellmann and Hu references utilize antisense nucleic acid molecules in methods of target specific inhibition. As stated above, and as evidenced by Moon, LaPlante, and Hu, those of ordinary skill in the antisense art understand that it is common to use transfection agents in antisense mediated in addition.

Finally, applicants argue that Gewirtz is not combinable with the Hellmann reference because Gewirtz is concerned with better efficiency of oligos and does not mention large circular stranded nucleic acids. However, Gewirtz was not relied upon for he teaching of large circular stranded nucleic acids, but for he teaching that antisense oligos are commonly utilized with transfection agents, a fact apparently conceded by applicants statement that at page 17 of their arguments: "transfection effective agents for nucleic acids were known in the art at the time of the invention as exemplified by Gewirtz". The reference of Gewirtz was cited to provide evidence that antisense nucleic acids with demonstrated inhibitory capacity, such as that taught by Hellmann, are commonly mixed with transfection agents, such as those claimed instantly by applicants.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392,

170 USPQ 209 (CCPA 1971). Applicants have conceded in their arguments on page 17 that each of the separate ingredients were in existence at the time of applicants filing. Applicants have not argued that Hellmann demonstrates antisense mediated target specific inhibition. As is made clear by Moon, LaPlante, and Hu, one of ordinary skill in the antisense art would understand that transfection effective agents are commonly used with antisense nucleic acids.

Applicants have asserted that the cited references fall short of the motivation for combining "because none of the cited references recognizes or appreciates that the effective usefulness of transfecting these large circular single-stranded nucleic acid molecules into eukaryotic cells." (Applicants arguments page 17). However, applicants claimed invention is not a method but a composition. Hellman teaches the use of a large, circular, single-stranded nucleic acid molecule comprising an antisense region to inhibit gene expression. While the experiments were done in a cellular homogenate, this does not mitigate the fact that the composition of Hellmann teaches all of the instantly claimed elements except for the transfection effective agent. Moon teaches the use of circular single-stranded nucleic acid molecules comprising an antisense region to inhibit gene expression *in cells*. LaPlante and Hu both teach transfection of antisense sequences into cells for the purpose of achieving gene specific inhibition of expression using transfection effective carriers. Gewirtz teaches that antisense mediated inhibition in cells is commonly achieved using transfection effective carriers.

In other words, any ordinarily skilled artisan in the antisense field would consider Hellmann's teaching of target specific inhibition using large circular single-stranded nucleic acids and understand, particularly in view of Moon, LaPlante, and Hu, who also teach antisense mediated inhibition using transfection effective carriers, to the instantly combinable given the

high degree of overlap between these references, and particularly the highly prevalent use of transfection effective carriers in methods of achieving antisense mediated gene inhibition.

The rejection is maintained.

No claims are allowed.

Conclusion

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz, Ph.D. whose telephone number is 571-272-0763. The examiner can normally be reached on 8:00-4:30 M-F.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached at 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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JD Schultz, PhD

JAMES SCHULTZ
PATENT EXAMINER